REMARKS

Applicants thank the Examiner for entering the amendment filed August 22, 2003.

With this amendment, Applicants cancel claims 9, 22, 24-25 and 30-37 without prejudice and reserve the right to pursue the subject matter of these claims in this or a related application. Applicants amend claims 21, 23, 26, 39 and 40 to clarify subject matter and add new claims 43-55. Applicants have rewritten independent claim 40 as two independent claims, as discussed below. Applicants add new dependent claims 48-51 to separately claim the various inflammatory disorders recited in independent claim 44. Applicants also add new independent claim 52 which recites a functional assay for the compounds used in the methods of the invention. Accordingly, claims 21, 23, 26-29 and 38-55 are now pending.

Support for the new claims and the claims amendments can be found in the specification and the original claims as filed. Specifically, exemplary support for each new claim is presented in the following table.

Claim(s)	Support
44, 47-51	Page 5, lines 19-22
45-46	Page 9, lines 1-7
52	Page 8, lines 20-28 and original claims 7 and 9
53-55	Page 5, lines 19-22

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Applicants submit that no new matter is introduced by the claim amendments and the new claims.

Allowable Subject Matter

Applicants thank the Examiner for pointing out that claims 40-42 would be allowable if rewritten in independent form to include all the limitations of the base claim and any intervening claims. Applicants note that claim 40 depends from alternatively either claim 38 or 39. Accordingly, Applicants have rewritten claim 40 as two independent claims, one that includes all limitations of claim 38 (amended claim 40) and the other that includes all limitations of claims 38 and 39 (new claim 44). Applicants believe that independent claims 40 and 44 and claims 41-43 and 45-51 depending therefrom are allowable in view of the claim amendments suggested by the Examiner and request entry as such.

35 U.S.C. § 112, first paragraph–Written Description

Claims 21, 23, and 26-29 and 38-39 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time this application was filed, had possession of the claimed invention. Specifically, while the Examiner acknowledges that the specification describes a method of treating using antibodies against the GM4,6D of SEQ ID NO:2 or 3, the Examiner contends that there is no evidence that there is any per se structure/function relationship between the disclosed modulator/inhibitor compounds in the genus. (Office Action at page 3).

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Applicants traverse this rejection in view of the following remarks, and respectfully request that this rejection be reconsidered and withdrawn.

The claimed invention, as recited in instant independent claim 21, is directed to a *method* for treating a subject having an inflammatory disorder characterized by aberrant GM4,6D polypeptide activity or aberrant GM4,6D nucleic acid expression by administering to the subject a GM4,6D modulator. Similarly, the claimed invention, as recited in instant independent claim 23, is directed to a *method* for modulating an inflammatory response in a subject by administering a GM4,6D modulator. Claim 38 is directed to a *method* for treating a subject having an inflammatory disorder characterized by excessive GM4,6D activity or excessive GM4,6D nucleic acid expression by administering an inhibitor of GM4,6D activity.

The fundamental factual inquiry in a written description rejection is whether the claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed.

At the time that the application was filed, Applicants had possession of the claimed *methods* for treating a subject having an inflammatory disorder by administering modulators or inhibitors of the disclosed GM4,6D polypeptides. Applicants submit that the focus of the inquiry should not be not whether Applicants have described every modulator/inhibitor that can be used in the claimed methods, but whether Applicants have adequately described the claimed methods. Applicants submit that a description of all species that a claim encompasses is not required to fulfill the written description requirement. *Utter v. Hiraga*, 845 F.2d 993, 998, 6 U.S.P.Q.2d 1709, 1714 (Fed. Cir. 1988).

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The specification as filed specifically discloses nucleic acid and polypeptide sequences for the GM4,6D polypeptides of the invention and also teaches in Example 2 various assays by which the activity of GM4,6D polypeptides can be measured. Additionally, the specification provides at least one screening assay that can be used to identify compounds that modulate GM4,6D activity, such as a compound or agent capable of inhibiting GM4,6D enzyme activity. (See specification as filed at page 8, lines 11-28). Accordingly, the specification as filed provides support for compounds or agents that modulates GM4,6D enzyme activity in one or more assays described by the Applicants, which can then be used in the methods of the claimed invention. While the specification specifically teaches antibodies to the disclosed GM4,6D polypeptides, as acknowledged by the Examiner, one skilled in the art would appreciate that the screening assays disclosed in the specification are not limited to the identification of antibodies that modulate GM4,6D activity but disclose the identification of any compound or agent which modulates GM4,6D activity. Thus, although the Examiner appears to contend that there is no evidence of a relationship between the disclosed modulator/inhibitor compounds in the genus, Applicants submit that compounds in the genus are related by virtue of their effect on GM4,6D activity in one or more assays taught by the Applicants. Applicants have added new claim 52 which specifically recites this assay.

As discussed above, at the time the application was filed, Applicants had possession of the claimed methods. The Office's written description rejection mistakenly overemphasizes the compositions used in the claimed methods instead of

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assessing whether the methods themselves are supported by the written description. Applicants are not claiming compounds which modulate/inhibit GM4,6D activity, but instead are claiming methods of treating inflammatory disorders by administering modulators/inhibitors of GM4,6D activity.

Applicants submit that the methods of the claimed invention are adequately described by the specification as filed. For example, the specification provides specific pharmaceutical compositions containing inhibitors identified by screening assays of the invention. (See specification at page 9, lines 8-29.) The specification also provides methods of administration of the inhibitors of GM4,6D activity identified by screening assays of the invention. (See specification at page 10, line 7 to page 11, line 20.) Furthermore, as discussed above, compounds or agents which are capable of modulating GM4,6D activity are related by virtue of their effect on GM4,6D activity in one more assays taught by the Applicants.

The written description requirement may be satisfied if the broader concept would naturally occur to one skilled in the art upon reading the specification. *In re Smythe*, 480 F.2d 1376, 1384, 178 U.S.P.Q. 279, 285 (C.C.P.A. 1973). Accordingly, having read the specification, the skilled artisan would recognize that Applicants possess compounds or agents which are capable of modulating GM4,6D activity in one or more assays provided by the Applicants. The skilled artisan would also recognize having read the specification that Applicants possessed methods of modulating an inflammatory response by administering a GM4,6D modulator, which can be identified using one or more assays disclosed in the specification.

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Accordingly, Applicants submit that a *prima facie* case of inadequate written description has not been established for claims 21, 23, 26-29 and 38-39, and request that this rejection be reconsidered and withdrawn.

35 U.S.C. § 112, first paragraph–Enablement

Claims 21, 23, and 26-29 and 38-39 are rejected under 35 U.S.C. § 112, first paragraph as allegedly non-enabled. The Examiner acknowledges that the specification is "enabling for a method of treating a subject with antibodies against the GM4,6D of SEQ ID NO:2 and 3." (Office Action at page 5.) The Examiner contends, however, that the specification "does not reasonably provide enablement for treating a subject with any modulators/inhibitors against GM4,6D or antibodies against GM4,6D different from SEQ ID NO: 2 and 3." (*Id.*)

The Examiner further contends that "[o]ne of ordinary skill in the art would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not have known how to make them. An assay for finding a product is not equivalent to a positive recitation of how to make a product." (Office Action at page 6.)

The test of enablement is whether one skilled in the art could make or use the claimed invention from the disclosures in the patent application coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 8 U.S.P.Q.2d 1217, 1222 (Fed. Cir. 1988). The law allows some reasonable experimentation, and does not require Applicants to disclose each embodiment of the claimed invention.

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Applicants submit that while some experimentation may be required to test known or unknown compounds or agents for their effect on GM4,6D activity, doing so is not enough to shift the burden to Applicants to prove that such experimentation is not undue.

First, the term "GM4,6D activity" is clearly defined in the specification as "the ability to convert GDP-mannose to GDP-4-keto-manose." (See page 5, line 12.) Second, the specification provides the following screening assay to identify compounds that inhibit GM4,6D activity:

> a first mixture is formed by combining a GM4,6D peptide of the present invention with GDP-mannose by such peptide, and the amount of conversion in the first mixture (B_0) is measured. A second mixture is also formed by combining the peptide, the substrate and the compound or agent to be screened, and the amount of conversion in the second mixture (B) is measured. The amounts of conversion in the first and second mixtures are compared, for example, by performing a B/B_0 calculation. A compound or agent is considered to be capable of inhibiting enzyme activity if a decrease in conversion in the second mixture as compared to the first mixture is observed.

(See page 8, lines 20-28.)

Third, Example 2 provides the three additional assays for measuring GM4,6D activity. Thus, the Applicants teach that inhibitors useful in the claimed methods of modulating GM4,6D activity may be also be identified by observing GM4,6D activity by:

> (1) incubation of radiolabeled ^{14}C or ^{3}H on unlabeled GDP-mannose in the presence of salts, buffers and cofactors with enzyme or enzyme extracts, and separation of the reactants and products by HPLC (for example, as described in Yamamoto et al. (1993) Archives of Biochemistry and Biophysics, vol. 300, 694-698) (See page 12, lines 27-31);

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> (2) coupling the reaction with the enzyme(s) GDP-4-keto-6-deoxy-mannose, epimerase, reductae [*sic*] and monitoring the coupled oxidation of NADPH using, for example, visible or fluorescent spectroscopy (for example, as described in Yamamoto et al., supra). (See page 12, line 31 - page 13, line 4); or
>
> (3) following the absorbance of the product GDP-4-keto-6-deoxy-mannose at 325 nm in alkali solution (for example, as described by Kornfled and Ginsberg (1966) Biochimica et Biophysica Acta, vol. 117, 79-87). (See page 13, lines 5-7.)

Thus, it would only be a matter of routine experimentation to identify GM4,6D modulators for use in the claimed methods. In view of the Applicants' teachings, the specification does enable the claimed methods for treating a subject having an inflammatory disorder characterized by aberrant GM4,6D activity or aberrant GM4,6D nucleic acid expression. Accordingly, Applicants submit that all of the pending claims are properly enabled by the instant specification.

35 U.S.C. § 112, second paragraph

Claims 21, 23, and 26-29 are rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite. According to the Examiner, the omitted elements from the claims are: the therapeutically effective amount of the antibodies/inhibitors/modulators needed to treat a subject having an inflammatory disorder. (Office Action at page 7.)

Applicants amend claims 21 and 23 to introduce the limitation " therapeutically effective amount." Accordingly, Applicants submit that each of the claims 21 and 23 and dependent claims 26-29, complies with the requirements of 35 U.S.C. § 112, second paragraph. Support for this amendment is found, for example, at page 9, lines 17 to page 10, line 6.

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Conclusion

In view of the foregoing amendments and remarks, Applicant respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims. Should the Examiner not believe that the claims are in conditions for allowance, Applicants request that the Examiner contact the undersigned representative at (617)452-1618 for an interview to discuss the application.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: February 18, 2004

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